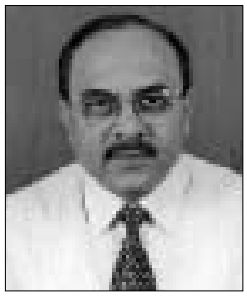

# Interstitial Lung Disease - Management

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Interstitial lung disease is a type of diffuse parenchymal lung disease due to heterogenous group of non-infectious, non-malignant processes of the lower respiratory tract that commonly result in restrictive ventilatory impairment, diffuse interstitial opacities, granulomatous or interstitial inflammation and fibrosis and it is often progressive and fatal. Commonest variety of diffuse interstitial lung disease is idiopathic interstitial pneumonia or cryptogenic interstitial pneumonitis.

Interstitial pneumonia signifies involvement of the lung parenchyma by varying combinations of fibrosis and inflammation in contrast to airspace disease typically seen in bacterial pneumonia. There are various problems in the diagnosis and management of these disorders especially as these conditions are uncommon and very few physicians or family physicians have substantial experience with their diagnosis and management.

There are many different causes of interstitial lung disease and they can be grouped in to five main groups. Those with known etiologies like drug-induced and occupational and environment, other systemic disorders like sarcoid or pulmonary hemorrhage or vasculitis, connective tissue diseases can have multiple systemic abnormalities of which interstitial pulmonary disease is one of them and the big group is idiopathic pulmonary fibrosis. All these injuries lead to lung fibrosis which can progress to end-stage fibrosis called "Honeycomb Lung".

Idiopathic interstitial fibrosis or usual interstitial pneumonia (IIP or UIP) is a histopathological pattern which can further be classified as nonspecific interstitial pneumonia (NIP), cryptogenic organizing pneumonia (BOOP), acute interstitial pneumonia (AIP) and desquamative interstitial pneumonia (DIP). IPF prevalence is 13-20 per 100,000 in US and the onset is usually between 50 and 70 years.

The clinical presentation is non-specific and consists of progressive dyspnoea on exertion, paroxysmal non-productive cough, fine, dry end-inspiratory crackles posteriorly in lower chest.

The presentation can be acute, subacute or chronic (Table 1)

Physical examination reveals crackles more often seen in inflammatory fibrotic disease and is rare in granulomatous lung disease. Other signs and symptoms are dependent on the underlying disease as skin changes are seen in scleroderma, joint deformities in arthritis. As the disease progresses there is clubbing and signs of cor pulmonale.

**Table 1 : Classification of Interstitial Lung Disease**

| |
|---|
| **Acute (day to weeks)** |
| Acute idiopathic interstitial pneumonia (AIP, Hamman-Rich syndrome) |
| Eosinophilic pneumonia |
| Hypersensitivity pneumonitis |
| Bronchiolitis obliterans with organising pneumonia |
| **Subacute (weeks to months)** |
| Sarcoidosis |
| Some drug-induced ILDs |
| Alveolar hemorrhage syndrome |
| Connective tissue disease |
| **Chronic (months to years)** |
| Idiopathic pulmonary fibrosis |
| Sarcoidosis |
| Pulmonary histiocytosis |

Blind studies are not helpful in diagnosing a particular disease. Most important are antinuclear cytoplasmic antibody in diagnosing Wegener's granulomatosis or vasculitis (ANCA), ANA, RF, angiotensin-converting enzyme (ACE) is nonspecific but may be useful in diagnosis of sarcoidosis.

Pulmonary function tests may give information about the type and extent of abnormality and may be useful in monitoring the response to treatment. The commonest pattern of lung function abnormality is restrictive impairment. There is marked increase in the flow of all lung volumes. The lungs are stiff and hence there is reduction in lung compliance. Diffusing capacity may be reduced due to loss of functioning alveolar capillary units.

Very low levels of TLCO (<40%) signify the presence of pulmonary hypertension. Arterial blood gas may show a normal or decreased partial pressure of arterial oxygen ($PaO_2$) with a widened alveo-arterial gradient ($PA\text{-}aO_2$). The hypoxemia may worsen during exercise.

There are two major histological patterns of diffuse parenchymal lung diseases (i) granulomatous process and (ii) interstitial inflammation and fibrosis. The causes of these are listed in Table 2 and 3.

Radiographically the chest radiograph shows bilateral lower zone nodular and reticular opacity or honeycombing. CT scan is very characteristic, shows bilateral, subpleural reticular opacities or honey-combing involving mainly the lower zones. Ground-glass opacity suggests alveolitis and the possibility of nonspecific interstitial pneumonias is likely.

**Table 2: Granulomatous Process**

- Sarcoidosis
- Organic dusts
  - Hypersensitivity pneumonitis
- Inorganic dusts
  - Beryllium
  - Silica
- Granulomatous vasculitides
  - Wegener's granulomatosis
  - Churg-Strauss

**Table 3 : Interstitial Inflammation and Fibrosis**

- Drugs (chemotherapy)
- Radiation
- Inorganic dusts (asbestos, fumes, gases)
- Collagen vascular disease
- Pulmonary hemorrhage syndromes
- Lymphocytic infiltrative disorders
- Eosinophilic pneumonias
- Idiopathic interstitial pneumonias (UIP, DIP, NSIP, BOOP)
- Inherited diseases (tuberous sclerosis)

The lung biopsy, either transbronchial or thoracoscopic, is useful to know the exact etiology in certain conditions. It should be considered when the CT scan shows a ground-glass opacity or air space consolidation. It may or may not be useful in following conditions (Table 4).

No data exists that adequately documents any of the current treatment approaches improves survival or improves quality of life for patients. Therapy should not be considered unless a definite diagnosis is established. The therapy is not indicated for all patients. If it is decided to treat the patients then it should be started on the first identification of clinical and physiologic evidence of impairment of documentation of decline in lung function.

The treatment of interstitial lung disease involves treatment of the systemic cause if any, removal of the offending agent if any. The treatment of lung involves anti-inflammatory drugs and supportive treatment. The effective anti-inflammatory treatment currently recommended is the combined therapy with corticosteroids and either azathioprine or cyclophosphamide.

Prednisone (or equivalent) is given in the dose of 0.5 mg/kg [lean body weight (LBW)] per day orally for 4 weeks followed by 0.25 mg/kg (LBW) per day for 8 weeks and then tapered to 0.125 mg/kg daily of 0.25 mg/kg every other day.

Azathioprine or cyclophosphamide is started with 2 mg/kg LBW per day orally. The dosing should begin at 25-50 mg/d and increase gradually by 25 mgm increments every 7 to 14 days until the maximum dose (100 to 150 mg/day) is reached. Newer drug approaches under consideration are which are currently under investigations but yet to prove their effective role in treatment of EPF are listed in Table 5.

**Table 4 : Usefulness of Transbronchial Lung Biopsy for Diagnosis of Interstitial Lung Disease**

| |
|---|
| Very useful |
| Sarcoidosis |
| Lymphangitic carcinomatosis |
| Alveolar proteinosis |
| Bronchioloalveolar carcinoma |
| Eosinophilic pneumonia |
| Berylliosis |
| Occasionally useful |
| Eosinophilic granuloma |
| Amyloidosis |
| Wegener's granulomatosis |
| Pulmonary lymphoma |
| Hypersensitivity pneumonitis |
| Lymphocytic interstitial pneumonia |
| Bronchiolitis obliterans organizing pneumonia |
| Not useful |
| Idiopathic pulmonary fibrosis |
| Other disease categories with underlying idiopathic interstitial pneumonitis |
| Non-specific interstitial pneumonias |

**Table 5: Future Therapies**

| |
|---|
| **Antifibrotic Agents** |
| Pirfenidone |
| Relaxin |
| Interferon-beta |
| Interferon-gamma |
| **Other Agents** |
| Acetylcysteine |

TNFR : FC (Enbrel ®, Etanercept – recombinant TNF receptor : Fc fusion protein : binds and inactivates TNF)